

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)



REC'D 03 FEB 2006

WIPO PCT

Applicant's or agent's file reference T2952-PCT	FOR FURTHER ACTION See Form PCT/PEA/416	
International application No. PCT/BE2004/000117	International filing date (day/month/year) 12.08.2004	Priority date (day/month/year) 12.08.2003
International Patent Classification (IPC) or national classification and IPC A61K38/19, A61P19/00		
Applicant TIGENIX N.V. et al.		

1. This report is the International preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
 - a. ☒ sent to the applicant and to the International Bureau) a total of 3 sheets, as follows:
 - ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
 - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
 - b. ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:
 - ☒ Box No. I Basis of the opinion
 - ☐ Box No. II Priority
 - ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - ☐ Box No. IV Lack of unity of invention
 - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - ☐ Box No. VI Certain documents cited
 - ☐ Box No. VII Certain defects in the international application
 - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand 01.06.2005	Date of completion of this report 05.12.2005
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Winger, R Telephone No. +49 89 2399-8129 

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/BE2004/000117

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-27 as originally filed

Claims, Numbers

24-31 as originally filed

1-23 received on 04.06.2005 with letter of 01.06.2005

Drawings, Sheets

1/2, 2/2 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/BE2004/000117

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- ☐ the entire international application,
 - ☒ claims Nos. 16, 18-22 (industrial applicability)
because:
 - ☒ the said international application, or the said claims Nos. 16, 18-22 (industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):
see separate sheet
 - ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
 - ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 - ☐ no international search report has been established for the said claims Nos.
 - ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
 - ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
 - ☐ See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/BE2004/000117

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-22
	No: Claims	23
Inventive step (IS)	Yes: Claims	1-19
	No: Claims	20-22
Industrial applicability (IA)	Yes: Claims	1-15,17,23
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Section III

1. Claims 16 and 18-22 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Section V

2. Prior Art: Reference is made to the following documents cited in the International Search Report
D1: US-A-5 786 217
D2: US-B1-6 410 268
D3: EP-A-1 312 614
D4: WUYTS ANJA ET AL: LABORATORY INVESTIGATION, vol. 83, no. 1, 23-34
D5: US 2002/123483 A1
D6: US-B1-6 413 511
 - 2.1 Document D1 discloses chondrogenic cells for the generation of cartilage.
 - 2.2 Document D2 discloses Ck α -3 (CXC-chemokine binding to the known IL-8 receptors) for the treatment of osteoarthritis along with the medical use of cells expressing it.
 - 2.3 Document D3 discloses the use of CXCL6 expressing cells in medicine.
 - 2.4 Document D4 discloses that human chondrocytes produce CXCL6 and that this production can be increased by LPS, poly rI:rC, IL-1b or TNF- α .
 - 2.5 Document D5 discloses CXCR-1 and CXCR-2 receptor ligands for the treatment of arthritis.
 - 2.6 Document D6 discloses modified chondrocytes for promotion of cartilage growth comprising growth factors.
3. Novelty (Article 33(2) PCT):
 - 3.1 Claim 1 relates to the use of CXCL6 for the promotion of cartilage and/or bone formation in vivo, claim 9 to the use of CXCL6 expressing cells comprising foreign DNA encoding said CXCL6, claim 16 to its use as marker, claim 17 to its in vitro use, claims 18 and 19

to chondrogenic stability and induction. As none of the prior art documents disclose such a use, the subject-matter of claims 1-19 seems to be novel.

- 3.2 Claim 20 relates to a method for producing a pharmaceutical for promoting cartilage and/or bone formation in vivo comprising a compound that increases the expression level of CXCL6. Notwithstanding the lack of clarity and sufficiency of disclosure, none of the prior art documents D1-D6 disclose such a use.
- 3.3 Claim 23 relates to a method for producing a medicament for the promotion of cartilage and/or bone formation in vivo comprising CXCL6 expressing cells. However, as documents D1-D4 (chondrocytes express CXCL6) disclose such uses, the subject-matter of claim 23 does not seem to be novel.

4. Inventive Step (Article 33(3) PCT):

- 4.1 Claim 1 relates to the use of CXCL6 for the promotion of cartilage and/or bone formation in vivo, claim 9 to the use of CXCL6 expressing cells comprising foreign DNA encoding said CXCL6, claim 16 to its use as marker, claim 17 to its in vitro use, claims 18 and 19 to chondrogenic stability and induction.
- Document D6, which can be regarded to represent the closest prior art document, differs in that a different polypeptide is used for cartilage induction. The problem to be solved can be regarded as to provide alternative polypeptides for cartilage induction. However, although document D2 discloses the use of CXCL6 for the treatment of osteoarthritis (via anti-inflammatory effects), there is no indication of a cartilage promoting effect, and therefore the subject-matter of claims 1-19 seems to be inventive.
- 4.2 Claim 20 relates to a method for producing a pharmaceutical for promoting cartilage and/or bone formation in vivo comprising a compound that increases the expression level of CXCL6. However, as it is not plausible that all CXCL6 inducing compounds are suitable for such a use (especially in view of the compounds of document D4) and as nothing has been shown for any inducer, the problem does not seem to have been solved (over the whole scope). Thus, the subject-matter of claims 20-22 does not seem to be inventive.

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/BE2004/000117